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The Uses and Limitations of the Miracle Drugs

A radio discussion over WGN and the Mutual Broadcasting System

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The Uses and Limitations of the Miracle Drugs

MR. McBURNEY: I am happy to present our speakers today: Dr. Robert D. Coghill, Director of Research and Member of the Board of Directors, Abbott Laboratories; Dr. Paul S. Rhoads, Professor of Medicine, The Medical School, Northwestern University, Chairman, Department of Medicine, Wesley Memorial Hospital, Chicago; and Dr. Guy P. Youmans, Chairman, Department of Bacteriology, The Medical School, Northwestern University.

As our announcer has just said, we are discussing the term "miracle drugs."

The term "miracle drugs" or "wonder drugs" seems to have wide use. What does it mean, Dr. Rhoads? What is your reaction to it?

'Unfortunate Term'

DR. RHOADS: Personally, I think the term "miracle drugs" is a very unfortunate one. I suppose that from the time the use of drugs began, and one drug after another was found to be effective against a given condition, it was hailed with great enthusiasm and the people called it a miracle drug, just as they talk of the drugs that we have now.

These drugs came into being as a result of hard and laborious procedures in the laboratories, in the medical schools, and at the bedsides. I am sure that the people who have developed them and made them so extremely useful at the present time would object to that term. I think that is the attiude of my friend Dr. Coghill, who is in charge of production of these drugs at Abbott Laboratories, and Dr. Youmans, who has done fundamental research on streptomycin in the laboratory.

MR. McBURNEY: Do you think that they are "miracle" drugs, Dr. Coghill?

Perhaps they are such in the terms of the results that they achieve.

DR. COGHILL: Those of us who develop and produce them realize that they are the result of careful planning and an awful lot of hard work. Every large pharmaceutical house has spent millions of dollars in research, and when we get out good ones we don't like them called miracle drugs.

'Wide Variety'

MR. McBURNEY: What kind of modern drugs are we talking about when we talk about these so-called miracle drugs, Dr. Youmans?

DR. YOUMANS: There are a wide variety of drugs used for medical work. These include, among many others, the antibiotics and such drugs as cortisone and insulin. However, I believe the antibiotics are most commonly referred to as "miracle drugs" and perhaps we should limit our discussion to these.

MR. McBURNEY: What do you mean by antibiotics?

DR. RHOADS: They are antibacterial substances that are produced by living microorganisms. They grow in culture media and are prepared in different ways before they are used in the body. When they are injected into the body or are taken by mouth, they have an effect which inhibits the growth of bacteria in the body. They make it harder for the bacteria to grow in a given spot in the body. Of course, the eventual finishing off of these bacteria is done by the defense forces of the body. There is an increase in the blood corpuscles and they gobble up the bacteria.

MR. McBURNEY: Let's get some of these antibiotics identified. I think that penicillin is the main one.

DR. YOUMANS: Yes, it was the first one—at least the first one that could be used practically. At the present time we also have streptomycin, aureomycin, terramycin, and chloromycetin and many others that are used for special purposes. We differentiate between antibiotics and sulfa drugs.

MR. McBURNEY: Where do these sulfa drugs fit into your classification?

DR. YOUMANS: They are also chemotherapeutic agents because their action is on the bacteria, but they are produced by the chemist in the laboratory whereas the antibiotics are produced by microorganisms. Their action is not on the patient himself. There are drugs which produce a physiological effect on the human being, but the antibiotics and sulfa drugs produce direct effects on the invading organisms producing the disease.

ACTH and Cortisone

MR. McBURNEY: What about ACTH and cortisone?

DR. RHOADS: By and large we feel it unsafe to use these preparations in treating infections.

MR. McBURNEY: Why?

DR. RHOADS: ACTH and cortisone give the patient a false sense of well being. They often bring the temperature down promptly and take away the aches and pains and the patient feels fine. But the infection will march on unless it is covered by quite large doses of antibiotics. As soon as we drop the ACTH and cortisone, the old symptoms reappear and we find that the infection has not gone away although the patient feels much better.

DR. YOUMANS: There is some evidence to indicate that cortisone may make some infections worse.

DR. RHOADS: That is true of tuberculosis.

MR. McBURNEY: In talking about these so-called miracle drugs today, I take it, then, that we are dealing primarily with these antibiotics. How are they produced, Dr. Coghill?

DR. COGHILL: First of all you have to discover the antibiotic. The source is generally in the soil. We get soils from all over the world. We can go to molds that are contained in the soils in such a way that they grow out in discrete colonies and then we can so conduct our experiments that we can pick out from these molds the ones that are active against tuberculosis or any other organisms in which we may be currently interested.

Contrary to what most people think, new antibiotics are relatively easy to discover. We discover dozens of them in a year. A new antibiotic is not a new drug. Certainly less than one per cent of the new antibiotics we discover have any usefulness at all.

Once we get them out, we have to get them in large enough quantities so that we can evaluate them. First we have to find out what they are good for, how to use them, and whether they are safe. That is our greatest responsibility, to be sure that we are not using as a drug a material which will have side effects. So we have to test them in animals and that animal testing is a tremendous job.

We have one department that does just that. There are over thirty people working continually the year around evaluating new drugs. In a year we use over 40,000 mice and over 15,000 rats, thousands of rabbits, and lesser numbers of dogs, cats, pigeons and other animals.

MR. McBURNEY: Do you conduct clinical trials?

Safety

DR. COGHILL: Our first responsibility is to determine the safety of the drug. We have to determine their greatest toxicity. What will it do immediately for the patient when you inject it? Or what will happen when

you give it to a patient every day for six months? Sometimes we run tests for a year and a half. We also have to determine what dosage to recommend. We have to find out how much gets into the blood and how long it stays there and also what side effects it produces.

When we have done enough of this work to assure ourselves that the drug is probably valuable in the treatment of some disease and relatively safe for the doctor to use, then we turn it over to some responsible physicians or research institutions for some preliminary clinical trials.

'Proceed with Caution'

DR. RHOADS: You can be sure that when these new antibiotics are offered to us they are received with the greatest enthusiasm, but, of course, we have to proceed with a great deal of caution.

First we go over all the material submitted to us by the drug house in question and see whether it is sound and reasonable. It usually is. Often we retest the antibiotic potencies in the test tube ourselves and sometimes in the laboratory and then proceed very cautiously with trials in human beings. Personally, I always get an assurance from the drug house in person that the drug has been used at least on a few human beings before we give it to the first person.

We do careful bacteriological studies on these people before and after treatment. We evaluate the clinical results and then prepare protocols of these trials which we return to the drug house and which they must submit to the Pure Food and Drug Bureau of the United States Public Health Service before they can get permission to put these things on the market for doctors generally.

Usually these clinical trials are made in medical centers throughout the country, which are separated widely geographically. They may present slightly different ideas, perhaps, in evaluation, so that there is a good cross section of opinion about them. The Pure Food and Drug people act upon that material.

MR. McBURNEY: I take it that these antibiotics are designed primarily to fight infection. That was brought out a little earlier. How do they do that job?

'Fight Infection'

DR. YOUMANS: I think that this was already pointed out. These agents have the unique property of inhibiting the multiplication of these microorganisms that produce disease. In other words, these bacteria, when they get into the body and produce disease, multiply and increase in number and during the course of the multiplication they produce substances which are injurious to the body and that is what gives the symptoms of the disease.

The antibiotics, I said, have the unique property of inhibiting the multiplication of these bacteria. Actually the uniqueness of their action is not so much in inhibiting multiplication of these organisms as it is in the fact that they will inhibit the multiplication of the bacteria within the body.

MR. McBURNEY: Do they work like iodine, for example?

DR. YOUMANS: Iodine actually kills the bacteria with which it comes into contact. These just combine with the bacteria and in some way which is unknown, keep them from multiplying.

DR. RHOADS: These chemicals (like iodine) that you are talking about are often too toxic for the body. They do things to the tissues that are worse than what the bacteria are doing.

DR. YOUMANS: That is what I meant when I said that it was a very unique thing for the agent to prevent multiplication within the body. Most agents are too toxic to be used as chemotherapeutic agents. It is important to remember that in the final analysis it is the body of the human being affected which eventually disposes of the bacteria.

MR. McBURNEY: How effective are these different kinds of antibiotics in dealing with infection, Dr. Rhoads?

Do you have to have a separate antibiotic for each infection?

DR. RHOADS: In general that is true. Not for every infection though. A bacteriologist could probably explain this better, but in general, bacteria are divided into two broad groups, depending on how they take a stain containing iodine; a stain that was invented by Dr. Gram years ago.

Those that take this stain and become well stained with it are called gram positives and those which do not take the stain are gram negative organisms.

In general, penicillin is more effective against gram positive organisms although it is not effective against all of them, and, in general, streptomycin, for instance, is more effective against the gram negative group.

Then there are the broad spectrum antibiotics. In that group are included aureomycin, terramycin, and chloromycetin. This group has a property of being effective against both kinds, but again not against all of them. Only long clinical trials have led us to know what can be expected of any given antibiotic.

MR. McBURNEY: Do you ever use two or three of these in combination?

Combinations of Drugs

DR. RHOADS: Often we do. We have found, for instance in tuberculosis, that of all the things now available to us, streptomycin is the most effective, but resistant forms do appear. Since these can be disposed of by one of the newer agents, we use them in combination.

In the infection of the upper respiratory tract we have no one agent that we can use that will be effective, but by using a combination we can fight it effectively. Undulant fever is another illustration of where we use a combination of streptomycin or aureomycin or streptomycin or one of the sulfa drugs, which seems to be more effective than using one drug alone. We have numerous instances of that.

DR. COGHILL: One of the big advantages of the use of combination is that it slows down the development of the resistance strains that are inherent in the mechanism.

MR. McBURNEY: What do you mean by "resistance?"

Resistance Strains

DR. YOUMANS: You can take a bacterium, for instance, of tuberculosis and give the patient streptomycin at certain concentrations and you may finally get strains which will resist thousands of times the concentration of streptomycin that would inhibit their growth in the first place.

MR. McBURNEY: Does that support the general apprehension, in taking penicillin for example, that after you have taken it two or three times you develop an immunity to it?

DR. COGHILL: The bacteria develop the immunity! There is a popular misconception here which should be corrected that the patient becomes immune. It is the bacteria causing the infection which become immune, or resistant to the antibiotics.

As resistance develops, the antibiotic may appear to have lost its effect, but it has lost its effect on the bacteria and the next time the patient is sick, that same antibiotic is apt to give just as good an effect as originally.

DR. RHOADS: What Dr. Coghill has just said points up the fact that antibiotics should never be used in a haphazard fashion. The doctor should know the microorganism which is the cause for the condition which he is treating and select the antibiotics which do the best job against that particular strain. Then he should give it in good full doses so that it not only partially inhibits the microorganism but knocks the infection out. If you just partially inhibit the growth of the microorganism in question, it can gain resistance and thus become a so-called resistant strain.

MR. McBURNEY: Are there any infections which do not respond to these antibiotics?

DR. COGHILL: There are quite a number of virus infections which we cannot do anything with. In general, they are a virus of very small size. They come in different sizes. The larger viruses can be handled by some of the current antibiotics, but in the case of the smaller ones, such as the virus causing polio and so on, we have nothing effective against these.

MR. McBURNEY: Do you think that you will have sometime?

DR. COGHILL: I am confident that we will, but I would hate to set a date for the achievement.

DR. RHOADS: We are not doing well at this time with the fungus infections.

MR. McBURNEY: What are they? Would athlete's foot be an example?

DR. RHOADS: Athlete's foot is one kind. Then there are a number of different fungus diseases that affect the lungs—actinomycosis and many others. Fungi affect the gastrointestinal tract and often they grow almost unopposed when we sterilize a given part of the body with antibiotics and become a problem, whereas they would not have become a problem had we not killed off the other bacteria.

MR. McBURNEY: Are you saying then that when you kill certain bacteria through the use of these drugs, you may create a condition favorable to other bacteria not too pleasant in their own right?

'Destroy Competition'

DR. RHOADS: That's right. By destroying competition among the bacteria, killing off a particular strain, often bacteria which are not inhibited by a given antibiotic may find it a favorable condition for growth and growth may actually be promoted.

DR. COGHILL: That is particularly true of the yeast. Most of the antibiotics are not effective against the yeast. As soon as you kill off all the other bacteria, that leaves all the food supply to the yeast and they start growing. In one case there is one antibiotic which stimulates the growth of the yeast.

DR. YOUMANS: It may not be generally realized that we normally in the body possess a lot of bacteria and most of them cause us no harm, but when by the use of antibiotics we suppress the growth or destroy certain types of microorganisms, others that are there then normally are able to grow. Competition between organisms tends to keep them limited in number and therefore we do not usually suffer from these infections.

Side Effects?

MR. McBURNEY: This leads me to inquire into the possible bad effects of the antibiotics. Do they have serious side effects, Dr. Rhoads?

DR. RHOADS: That matter of dislocation of the normal bacterial floor of different parts of the body we have already gone into. That certainly is one of the possible bad side effects, but there is not a single antibiotic for which some unpleasant side effects are not present. I would say that with penicillin, allergic reactions are by all odds the most common reactions we encounter. About one per cent of the people who have penicillin injections put into them may develop hives or generalized itching or redness of their eyes and so forth. They are much more apt to get such reaction after a second injection.

Aureomycin and terramycin do not usually have very serious side effects, but they may cause some vomiting or they may initiate a protracted diarrhea.

Chloromycetin, in a few instances, has been found to have a bad effect on the blood forming organisms of the body.

Then there are others which are not in such common use. Examples would be neomycin and bacitracin and tyrothricin, which may have a very definite side effect on the kidneys.

MR. McBURNEY: Those side effects don't sound very pleasant.

DR. RHOADS: The doctor who uses the drugs must know about the possible effects, and they should never be used unless the good that can be expected can outweigh the possible bad effects. Fortunately, the bad effects do not occur very often.

MR. McBURNEY: Do different patients react differently to these drugs?

DR. RHOADS: Very definitely they do. The majority of people get along very well with them, but some of the more allergic are apt to have a bad time with them.

Uniformity of Drugs

MR. McBURNEY: Dr. Coghill, how uniform are the batches of these drugs as they come out? Could a lack of uniformity in the drug explain in part why patients react differently?

DR. COGHILL: In the early days there was a certain amount of lack of uniformity. The penicillin that caused all those effects that got it the name of a miracle drug was about five per cent penicillin and about ninety-five per cent impurities. Today it is the reverse—it is ninety-five per cent penicillin and the impurities are very minor. That also applies to the other antibiotics. Practically all of them today are being sold as pure chemicals.

DR. RHOADS: I would agree with that.

MR. McBURNEY: How many of these antibiotics do you manufacture in America in a year?

DR. COGHILL: Quite a lot. I don't think that we have mentioned production as yet.

The bacteria are put in large tanks, anywhere from five to thirty thousand gallons, and at the end of the growth you may have a solution of anywhere from one part in a thousand to one part in ten thousands of the antibiotic itself—a very costly operation.

This year it appears that we will produce in the United States about 225 tons of penicillin, about 240 tons of streptomycin and about 300 tons of the so-called broad spectrum antibiotics. The total will be somewhere between 750 and 800 tons this year.

MR. McBURNEY: How much do you usually give to a patient? Something less than a ton, I take it. (Laughter)

DR. RHOADS: Considerably less than a ton—from a tenth of a gram to a gram. That is a very small part of a pound, I assure you.

Cost of Penicillin

DR. COGHILL: In 1943 one hundred thousand units of penicillin sold for twenty dollars. Today you can buy that twenty dollars worth of penicillin for ten cents. Even then it is an expensive chemical.

MR. McBURNEY: What have these antibiotics done for humanity?

DR. YOUMANS: They have changed the whole area of the practice of medicine with regard to the bacterial diseases. They have resulted in the successful treatment of the vast majority of the bacterial diseases. Attaining a goal such as that has been the dream of medicine for many years, and now we have at least realized it in part.

Suggested Reading

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and M. Helen Perkins, Reference Department,
Deering Library, Northwestern University.

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What cortisone and ACTH can mean to a family's health, their effect in certain diseases, and their dangers.

Consumer Reports 16:474-5, Oct., '51. "Antibiotics."

The revolutionary effect of antibiotics on many bacterial and rickettsial diseases with a warning as to the dangers connected with using them unadvisedly.

Consumer Reports 16:141-76, Dec., '51. "1951 Buying Guide Issue; Drugs and Medicines."

A brief, concise statement as to the type of disease against which the various antibiotics are effective.

Consumers Research Bulletin 29:10, Mar., '52. "Caution Necessary with New and Unfamiliar Drugs."

A discussion of the harmful effect of various drugs, including some of the antibiotics.

Consumers Research Bulletin 28:21-2, Aug., '51. "Antibiotics: Penicillin and Others." E. DI CYAN.

A general description of the effectiveness and limitations of antibiotics.

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The story of the medical research which preceded the use of cortisone.

Fortune 45:118-21, Mar., '52. "Antibiotics in the Barnyard."

The extraordinary story of the work of the research teams who discovered that approximately 200 pounds of manufactured B12 could replace, for the feeding of farm animals, the natural B12 normally contained in a billion pounds of meat and fish by-products.

GP (General Practitioner) 5:67-78, Feb. '52. "The Antibiotics—Uses and Abuses."

Shows the care that must be taken in administering antibiotics.

Harper's Magazine 203:56-62, Sept., '51. "Cortisone and Plenty of It."

The place of cortisone in medicine, and the history of the expeditions sent out to discover new materials for its production.

Hygeia 25:776-7, Oct., '47. "Resistance to Infection." P. S. RHOADS.

A general article on the factors involved in the human body's resistance to infection and how this resistance can be heightened by the use of certain chemicals.

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A description of some of the results acheived through cortisone and ACTH.

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Emphasizes the fact that although there are more uses for the wonder drugs, there are increasing reports of germs developing resistance to them.

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An announcement that penicillin can be effectively used against bejel, which afflicts women and children in Arab lands, yaws, and pinta, the spotted disease of the Western Hemisphere.

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The beneficial influence of penicillin therapy in reducing the mortality of experimental animals receiving both burns and radiation shows the need of provision of this therapy for victims of atomic bomb attacks.

Science 116:282-4, Sept. 12, '52. "Effect of Terramycin and Aureomycin on Blood Coagulation." J.W.PARKER, JR. and L. T. WRIGHT.

A technical article with charts showing the clotting time of blood before and after injections, and the types of cases treated with aureomycin and terramycin.

Science News Letter 61:67, Feb. 2, '52. "Find First Antibiotic That Stops Trypanosomes: X 948."

A brief notice of the discovery of an antibiotic which will stop African sleeping sickness in animals, but which proved toxic to use on human beings.

Science News Letter 61:159, Mar. 8, '52. "Miracle Drugs in Foods."

Everyday foods containing small amounts of antibiotics do not appear to harm human beings.

Science News Letter 62:125, Aug. 23, '52. "Rules for Chloromycetin."

Why chloromycetin should be used according to government experts and why it should be used with care.

Scientific American 186:49-57, Apr., '52. "Progress of Antibiotics." K. B. RAPER.

An interesting history of the discovery of antibiotics, with a chart showing the effectiveness of penicillin, aureomycin, streptomycin, and chloramphenicol on various diseases.

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Because of several deaths attributed to chloromycetin, physicians urge extreme care in its use.

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What ACTH, cortisone, and other hormones can do to help combat various diseases.

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A warning against attempting to treat yourself with any of the antibiotics.

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Government officials answer questions in regard to the safety of using antibiotics.